PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Lei Yu

Serial No.: 09/626,616

Filed: July 27, 2000

For: METHODS OF SCREENING FOR SUBSTANCES WHICH BIND OPIOD RECEPTORS

Group Art Unit: 1647

Examiner: R. Landsman

Atty. Dkt. No.: INDA:005USD1

APPEAL BRIEF

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Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Commissioner:

Appellant hereby submits an original and two copies of this Appeal Brief to the Board of Patent Appeals and Interferences in response to the final Office Action dated December 31, 2002 ("the Action"). By virtue of the Request for Extension of Time submitted herewith, this brief is due on November 4, 2003 (the Notice of Appeal having been received by the PTO on June 4, 2003). The fee for filing this Appeal Brief is attached. If the check is inadvertently omitted, or should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed material, or should an overpayment be included herein, the Commissioner is

authorized to deduct or credit said fees from or to Fulbright & Jaworski L.L.P. Account No.: 50-1212/INDA:005/MBW.

I. REAL PARTY IN INTEREST

The real party in interest is the assignee, Advanced Research and Technology Institute.

II. RELATED APPEALS AND INTERFERENCES

There are no appeals or interferences related to this case.

III. STATUS OF THE CLAIMS

Claims 83-101 are currently pending. Claims 83-85 are allowed. Claims 91 and 100 are objected to as being allowable, but dependent upon non-allowed claims. Therefore, claims 91 and 100 have been indicated to be allowable if rewritten in independent form. Claims 86-90, 92-99, and 101 are rejected. A copy of the pending claims is attached as Appendix A to this brief.

IV. STATUS OF AMENDMENTS

No amendments have been filed after the Final Office Action.

V. SUMMARY OF THE INVENTION

The present invention is drawn to processes of screening a candidate substance for its ability to bind to an opioid receptor by contacting the candidate substance with an opioid receptor. Specification at p. 17, ln. 12-23. The opioid receptor can be a mu opioid receptor comprising the contiguous amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:8, or SEQ ID NO:17. Specification at p. 10, ln. 11-17. In some embodiments, the opioid receptor can be a mu opioid receptor encoded by a nucleic acid sequence comprising the contiguous nucleotide sequence of SEQ ID NO:7. Specification at p. 10, ln. 17-20. In other embodiments

the opioid receptor can be a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 35, 45, 50, 75, 100 or more contiguous nucleotides of SEQ ID NO:7. Specification at p. 12, ln. 3-15.

VI. ISSUES ON APPEAL

Are claims 86-90, 92-99, and 101 supported by the specification under 35 U.S.C. § 112, first paragraph?

Are claims 86-90, 92-99, and 101 enabled under 35 U.S.C. § 112, first paragraph?

Are claims 86-90, 92-99, and 101 definite under 35 U.S.C. § 112, second paragraph?

VII. GROUPING OF THE CLAIMS

The claims do not stand and fall together. Claims 83-85 have been allowed as indicated in the Action; therefore, they are separately patentable. Additionally, the subject matter in claims 91 and 100 is indicated to be allowable if redrafted in independent format. Therefore, claims 91 and 100 should stand and fall separately from the other claims.

VIII. ARGUMENT

A. The Claims Are Supported by the Specification Under 35 U.S.C. § 112, First Paragraph

Claims 86-90, 92-99, and 101 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that is not sufficiently described in the specification. The Examiner asserts that the specification fails to describe the common attributes and characteristics of claims that read on proteins encoded for by at least 35 contiguous bases of SEQ ID NO: 7, and which must include the guanine at position 389 of SEQ ID NO: 7. As such, the Examiner argues that the Appellant was not in possession of the claimed genus at the time the invention was made. The Board should overturn this rejection, which is not founded on fact or law.

1. *Appellant was in Possession of the Claimed Polypeptides at the Time the Invention was Made*

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991). The Examiner has stated that the written description is sufficient to demonstrate that Appellant was in possession of an opioid receptor encoded by SEQ ID NO: 7. The Action, p. 3. The rejected claims all recite portions of SEQ ID NO: 7. However, portions of a full-length sequence must themselves be described by the specification when the specification sets forth the entire sequence of the cDNA (SEQ ID NO: 7) and the corresponding protein (SEQ ID NO: 8), as is the case here.

In addition, all of the rejected claims have the limitation of including the guanine nucleotide at position 389 of SEQ ID NO: 7. One skilled in the art would reasonably conclude that the inventor had possession of a recombinant opioid receptor polypeptide encoded for by a nucleic acid sequence comprising at least 35 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7 based on the description provided for in the specification at least on pages 36 to 44; pages 150-153, and by SEQ ID NO:7 and SEQ ID NO:8.

2. *The Examiner Improperly Reads Limitations into the Claims*

Each claim must be separately analyzed and given its broadest reasonable interpretation, see, *e.g.*, *In re Morris*, 127 F.3d 1048, 1053-54 (Fed. Cir. 1997). Appellant asserts that the Examiner, in requiring that the "recombinant opioid receptor polypeptide" recited in the claims be a full-length opioid receptor, has not only failed to broadly interpret Appellant's claims, but has improperly interpreted the claims in an unreasonably narrow manner.

Appellant notes that the claimed invention is drawn to processes of screening a candidate substance for its ability to bind an opioid receptor. The Examiner argues that the process requires a full-length, functional mu opioid receptor. The Action, p. 3. Appellant asserts that the Examiner has improperly defined the claimed invention. None of the claims require that the process for screening a candidate substance utilize a full-length, functional mu opioid receptor. For example, claim 86 reads (emphasis added):

> A process for screening a candidate substance for its ability to bind to a mu opioid receptor comprising:
>
> (a) providing a ***recombinant opioid receptor polypeptide*** encoded by a nucleic acid sequence comprising at least 35 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7;
>
> (b) contacting the ***candidate substance*** with the recombinant opioid receptor polypeptide; and
>
> (c) detecting the ability of the candidate substance to ***bind*** to the recombinant opioid receptor polypeptide.

The recombinant opioid receptor polypeptide may be full length and may be functional, but this is not a requirement of the claim. The Examiner has, therefore, improperly read a limitation into the claims.

In making the written description rejection, the Examiner appears to be asserting that since the claim language includes "opioid receptor," that by necessity a full-length opioid receptor is required to practice the claimed invention. Such an interpretation is faulty and erroneous. In particular, the Examiner appears to be misinterpreting the requirements of written description set forth in *University of California vs. Eli Lilly and Co.*, which requires that claims to genetic material require recitation of more than a mere function. *University of California v. Eli Lilly and Co.*, 119 F.3d 1559 (Fed. Cir. 1997) ("In claims to genetic material, however, a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without

more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.") While it is true that in claims to genetic material, a generic statement without more is not an adequate written description of the genus, Appellant asserts that the claims are not for ***opioid receptors***, but rather are for ***processes of screening substances for the ability to bind to an opioid receptor***.

Appellant strongly asserts that the application is fully in compliance with the written description requirements set forth in *Eli Lilly* because the claimed process of screening utilizing polypeptides encoded by at least 35 contiguous bases of SEQ ID NO:7, including the guanine at nucleotide 389 of SEQ ID NO:7, is fully supported by the specification, particularly since SEQ ID NO:7 is disclosed in the application and one of skill in the art would be able to practice the claimed invention based on the existing disclosure.

The Examiner also reasons that the specification provides no written description as to what amino acid residues are necessary for a candidate substance to bind an opioid receptor. The Action, p. 3; Office Action dated May 30, 2002, p. 5. Again, Appellant notes that the claims are directed to a process of screening a candidate substance for the ability to bind an opioid receptor. Thus, the amino acid residues necessary for opioid function are not at issue as it relates to written description for claims 86-90, 92-99, and 101.

Furthermore, Appellant submits that there is nothing in the claim that limits the candidate substance to a ***ligand***, as suggest by the Examiner. Office Action dated May 30, 2002, p. 5. The claims recite a process for screening a "***candidate substance***." (see claim 86, above). Although a candidate substance may be a ligand, the claims do not require that the candidate substance be a ligand nor do they require that the binding occur only at the amino acid residues necessary for ligand binding. For example, the process may identify an antibody that binds a recombinant

opioid receptor polypeptide encoded for by a nucleic acid sequence of 35 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7.

In view of the Examiner's assertion that the rejected claims read on full-length recombinant opioid receptor polypeptides, Appellant would be willing to enter claims that replace the recitation "recombinant opioid receptor polypeptide" with "polypeptide," if the Board believes that this would clarify the fact that the polypeptide does not have to be a full-length opioid receptor.

3. Summary

In summary, the claims are directed to processes of screening a candidate substance's ability to bind to a recombinant opioid receptor polypeptide, which is defined as comprising a polypeptide encoded by a nucleic acid sequence comprising at least 35 nucleotides of SEQ ID NO:7, including the guanine at 389 of SEQ ID NO:7 (a distinguishing characteristic of the mu opioid receptor of the present invention), and not to mu opioid receptors *per se*. The pending claims are described in such a manner as to reasonably convey to one skilled in the art, at the time the application was filed, that the inventor was in possession of ***a process to screen a candidate substance for its ability to bind a recombinant opioid receptor polypeptide***. Accordingly, for the above reasons, Appellant contends that the claims are adequately described in the specification as filed and request that the Board overturn the rejection.

B. The Claims Are Enabled Under 35 U.S.C. § 112, First Paragraph

Claims 86-90, 92-99, and 101 stand rejected for lack of enablement under 35 U.S.C. § 112, first paragraph. The Examiner argues that Appellant has provided no guidance and working examples of full-length opioid receptors other than that encoded for by SEQ ID NO: 7. The Board should overturn this rejection, which is not founded on fact or law.

1. The Legal Standard of Enablement

To be enabling within the meaning of 35 U.S.C. § 112, the application must contain a description sufficient to enable one skilled in the art to make and use the claimed invention without unduly extensive experimentation. *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984). Furthermore, it is well settled that the Examiner has the initial burden of producing reasons that substantiate a rejection based on lack of enablement. See, *In re Marzocchi*, 439 F.2d 220, 224 (C.C.P.A. 1971); *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). The Examiner's burden requires that the Examiner supply a factual basis or scientific principle to reasonably doubt the accuracy of a clear disclosure. *In re Marzocchi*, 439 F.2d at 224.

Appellant submits that the application contains sufficient description to enable one skilled in the art to make and use the claimed invention without unduly extensive experimentation. The Examiner has not met his burden of producing reasons that substantiate a rejection based on lack of enablement. Rather, the Examiner's rejection appears to be based on an improper interpretation of the claims.

2. The Examiner Improperly Reads Limitations Into the Claims

The Examiner alleges that the claims "read on any ***full-length*** opioid receptor comprising at least 35 contiguous bases of SEQ ID NO:7." The Action, p. 3 (emphasis added). The Examiner further argues, "Therefore, then [*sic*] artisan would not know how to make a full-length receptor for use in the claimed method other than that encoded for by SEQ ID NO:7." The Action, p. 4. As stated above, the claims are directed to processes of screening a candidate substance for the ability to bind an opioid receptor. The claimed processes ***do not*** require that the recombinant opioid receptor polypeptide be a full-length opioid receptor. Rather, the claims provide a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence

comprising at least 35 contiguous nucleotides of SEQ ID NO:7, including the guanine at nucleotide 389 of SEQ ID NO:7.

Furthermore, the specification teaches the making and using of recombinant opioid receptor polypeptides, particularly chimeras, at least on pages 36–44. Also, numerous references cited within the specification describe methods of manipulating G-protein receptors known to those of skill in the art, such as adrenergic receptors. Thus, the preparation and use of a wide variety of recombinant opioid receptor polypeptides encoded by a nucleic acid sequence comprising at least 35 contiguous nucleotides of SEQ ID NO:7, including the guanine at nucleotide 389 of SEQ ID NO:7, was taught or known to one of skill in the art. The Examiner must presume the specification is enabling unless he can provide reasons to doubt the presumption. Here, no such reference or evidence is provided. The Examiner has not met his burden of providing ***any*** basis for rejecting the claims as not enabled, other than he does not agree with the Appellant's specification.

3. Summary

In summary, the claims are directed to processes of screening a candidate substance's ability to bind to a recombinant opioid receptor polypeptide, which is defined as comprising a polypeptide encoded by a nucleic acid sequence comprising at least 35 nucleotides of SEQ ID NO:7, including the guanine at nucleotide 389 of SEQ ID NO:7 (a distinguishing characteristic of the mu opioid receptor of the present invention), and not to opioid receptors *per se*. Appellant submits that the application contains sufficient description to enable one skilled in the art to make and use the claimed invention without unduly extensive experimentation. The Examiner has not met his burden of producing reasons that substantiate a rejection based on lack of enablement. Rather, the Examiner's rejection appears to be based on an improper interpretation of the claims.

Accordingly, for the above reasons, Appellant contends that the claims for the screening of a candidate substance for its ability to bind an opioid receptor are enabled by the specification and request that the Board overturn the rejection.

C. The Claims Are Definite Under 35 U.S.C. § 112, Second Paragraph

Claims 86-90, 92-99, and 101 are rejected under 35 U.S.C. § 112, second paragraph. The Examiner asserts that it is unclear whether the word "including" modifies the phrase "at least 35 contiguous nucleotides of SEQ ID NO:7." Appellant traverses this rejection.

As previously described to the Examiner in Appellant's response to the Office Action dated May 30, 2002, claim 86 states in part: "...providing a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 35 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7...". The word "including" modifies the phrase "at least 35 contiguous nucleotides of SEQ ID NO:7", and thus the guanine at nucleotide position 389 is included within the "at least 35 contiguous nucleotides of SEQ ID NO:7."

Accordingly, Appellant contends that the claims are definite and requests that the Board overturn the rejection.

IX. CONCLUSION

It is respectfully submitted, in light of the above, that all claims are in condition for allowance. Appellant, therefore, requests that the Board overturn each of the pending grounds for rejection.

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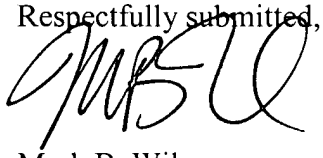
Respectfully submitted,



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Date: November 4, 2003

APPENDIX A

83. A process of screening a candidate substance for its ability to bind to a mu opioid receptor comprising:

a) providing a recombinant mu opioid receptor polypeptide comprising the contiguous amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:8, or SEQ ID NO:17; and

b) testing the ability of said candidate substance to bind to said opioid receptor.

84. The process of claim 83 wherein the step of testing the ability of the candidate substance to bind to the opioid receptor involves determining the binding affinity of the candidate substance to the receptor.

85. The process of claim 83, wherein the step of testing the ability of the candidate substance to bind to the opioid receptor involves determining the ability of the candidate substance to activate the receptor.

86. A process for screening a candidate substance for its ability to bind to a mu opioid receptor comprising:

(a) providing a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 35 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7;

(b) contacting the candidate substance with the recombinant opioid receptor polypeptide; and

(c) detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide.

87. The process of claim 86, wherein the nucleic acid sequence comprises at least 45 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7.

88. The process of claim 86, wherein the nucleic acid sequence comprises at least 50 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7.

89. The process of claim 86, wherein the nucleic acid sequence comprises at least 75 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7.

90. The process of claim 86, wherein the nucleic acid sequence comprises at least 100 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7.

91. The process of claim 86, wherein the nucleic acid sequence comprises the nucleotide sequence of SEQ ID NO:7.

92. The process of claim 86, wherein detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide involves measuring (i) the ability of the recombinant opioid receptor polypeptide to bind the candidate substance; (ii) the ability of the candidate substance to activate ion channels in a cell membrane; or (iii) modulation of ion channels in the cell membrane of part (ii).

93. The process of claim 86, wherein recombinant opioid receptor polypeptide is chimeric.

94. A process for screening a candidate substance for its ability to bind to an opioid receptor comprising:

(a) expressing a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 35 contiguous bases of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7;

(b) contacting the candidate substance with the recombinant opioid receptor polypeptide; and

(c) detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide.

95. The process of claim 94, wherein the nucleic acid sequence comprises at least 40 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7.

96. The process of claim 94, wherein the nucleic acid sequence comprises at least 45 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7.

97. The process of claim 94, wherein the nucleic acid sequence comprises at least 50 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7.

98. The process of claim 94, wherein the nucleic acid sequence comprises at least 75 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7.

99. The process of claim 94, wherein the nucleic acid sequence comprises at least 100 contiguous nucleotides of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7.

100. The process of claim 94, wherein the nucleic acid sequence comprises the nucleotide sequence of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7.

101. The process of claim 94, wherein recombinant opioid receptor polypeptide is chimeric.